REMARKS

In the Office Action of May 7, 2003, Claims 18 and 35 - 48 were rejected. Claims 17 and 28 - 34 are withdrawn from consideration. No claim was allowed. In response, Claims 37 and 39 - 41 are canceled without prejudice or disclaimer, Claims 18, 42 and 43 are amended. Reexamination and reconsideration are respectfully requested in view of the foregoing amendments and the following remarks.

Rejection of Claims 29 - 30, 36 - 37, 45 and 48 under 35 U.S.C. §112, second paragraph

Claims 29 - 30, 36 - 37, 45 and 48 are rejected under 35 USC 112, second paragraph, as being indefinite. The Examiner alleges that with respect to the recitation of phospholipase, it is unclear as to what phospholipase the claims are referring to. The Examiner alleges that there are different phospholipases, A and D, for example. The Examiner further alleges that the function of one of the phospholipases is to remove the phosphate head group and that when this is removed the lipid is not longer a phospholipid. The Examiner alleges that the specification does not adequately define the term.

This rejection is respectfully traversed as it may be applied to Claims 36, 45 and 48. (Claims 29 - 30 being withdrawn from consideration and Claim 37 having been canceled in the previous response.). In particular, it is respectfully submitted that the phrase "wherein the phospholipid is enzyme-modified lecithin obtainable by treating lecithin with phospholipase" would not be unclear to persons skilled in the art, since persons skilled in the art would have been aware, before the filing date of the application, that a phospholipid hydrolysis product may be obtained by treating soybean lechithin with

phospholipase A or phospholipase D. Such a product is described, for example, in U.S. Patent No. 4,478,866. A person skilled in the art would have clearly recognized that the phrase does not contemplate the use a phospholipase (phospholipid C) that does not produce a phospholipid. Therefore, the meaning of the claims would not have been unclear or indefinite to a person skilled in the art.

Accordingly, withdrawal of the rejection of Claims 36, 45 and 48 as being indefinite under 35 USC 112, second paragraph, is respectfully requested.

Rejection of Claims 18 and 35 - 48 under 35 U.S.C. §103(a) over Sugano (J. Nutr., 1990) or Sugano (Atherosclerosis, 1988) by themselves or in combination with Imaizumi

Claims 18 and 35 - 48 were rejected under 35 U.S.C. §103(a) as obvious over Sugano (J. Nutr., 1990) or Sugano (Atherosclerosis, 1988) by themselves or in combination with Imaizumi (Agri. Biol. Chem. 53 (9), 1989). The Examiner alleged that the Sugano references teach the effectiveness of soybean protein-phospholipid complexes in lowering cholesterol levels. The Examiner acknowledges that the amounts of phospholipids in Sugano are lower than the amounts in the present invention. The Examiner alleges that Imaizumi teaches that the administration of phospholipids causes the reduction in the serum cholesterol levels.

This rejection is traversed.

As discussed in Applicant's response of December 2, 2003, it is discovered in the present invention that a protein/phospholipid complex or protein hydrolyzate/phospholipid complex in which the content of bound phospholipid is from 20 to 50 wt% significantly

improves cholesterol metabolism of an animal, compared with a complex in which the content of bound phospholipid is 10 wt% or less.

As discussed in the previous response, both of the Sugano publications focus on the effect of reducing serum and liver cholesterol by an undigested high molecular fraction of soybean protein obtained after microbial protease digestion. However, contrary to what is alleged by the Examiner, the references do not teach that the effect is due to the complex of protein and phospholipid.

Imaizumi teaches that administration of phospholipids causes reduction of cholesterol levels in serum. However, the reference is silent as to whether the effect would be improved if the concentration of phospholipid were to be varied.

Therefore, the combination of Sugano, Sugano and Imaizumi does not teach or suggest the unexpected result of the present invention that the cholesterol metabolism of an animal can be improved by using the complex of the present invent ion in which the content of bound phospholipid is from 20 to 50 wt%.

With respect to the further allegations of the Examiner that the criticality of the enzyme modified phospholipid is not readily apparent and that the specification does not provide a definition or experiments conducted with enzyme modified phospholipid, it is respectfully submitted that the enzyme modified lecithin is defined clearly on page 2, lines 30-34 of the present specification. Further, in Test Example 1 of the present specification, there is an example of the complex obtained by using enzyme-modified lecithin in which the content of bound phospholipid is 20 wt%, shown as Group 4, in which enzyme-modified lecithin is used as "Elmizer AC". As shown in Table 2 of the present specification, "Total Cholesterol Concentration in Liver" of Group 4 is clearly lower than that of Group 1(isolated soybean protein) and Group 2(mixture of isolated soybean protein

and soybean lecithin) and Group B (isolated soybean protein/soybean lecithin complex in which the content of bound phospholipid is 20 wt%). That is, the effect of the complex obtained by using enzyme-modified lecithin is greater than that of a complex obtained by using enzyme unmodified-lecithin.

Accordingly, it is respectfully submitted that Claims 18 and 35 - 36, 38 and 42 - 48 are not obvious over the Sugano references or Imaizumi, alone or in combination.

Rejection of Claims 18 and 35 - 48 under 35 U.S.C. §103(a) over Sugano (J. Nutr., 1990) or Sugano (Atherosclerosis, 1988) by themselves or in combination with Imaizumi and further in view of Jenkins

Claims 18 and 35 - 48 were rejected under 35 U.S.C. §103(a) as obvious over Sugano (J. Nutr., 1990) or Sugano (Atherosclerosis, 1988) by themselves or in combination with Imaizumi (Agri. Biol. Chem. 53 (9), 1989) and further in view of Jenkins (Nutritional Reports International, 1983). The Examiner alleged that the Sugano references teach the effectiveness of soybean protein-phospholipid complexes in lowering cholesterol levels. The Examiner acknowledges that the amounts of phospholipids in Sugano are lower than the amounts in the present invention. The Examiner alleges that Imaizumi teaches that the administration of phospholipids causes the reduction in the serum cholesterol levels.

This rejection is traversed. As discussed above, both of the Sugano publications focus on the effect of reducing serum and liver cholesterol by an undigested high molecular fraction of soybean protein obtained after microbial protease digestion. However, contrary to what is alleged by the Examiner, the references do not teach that the effect is due to the complex of protein and phospholipid. Imaizumi teaches that

administration of phospholipids causes reduction of cholesterol levels in serum. However, the reference is silent as to whether the effect would be improved if the concentration of phospholipid were to be varied. Therefore, the combination of Sugano, Sugano and Imaizumi does not teach or suggest the unexpected result of the present invention that the cholesterol metabolism of an animal can be improved by using the complex of the present invent ion in which the content of bound phospholipid is from 20 to 50 wt%.

The Examiner's allegations that Jenkins discloses the effects of dietary protein and lecithin in plasma lipids, lipoproteins and cholesterol and teaches that the level of dietary lecithin controls the effect of the source and type of protein on the lipid metabolism may be rebutted as follows: In Table III of Jenkins, although cholesterol level of liver decreased (4.54mg/g) when 2.5% lecithin was fed with soy protein, the cholesterol level was not further decreased (4.70mg/g) even when the concentration of lecithin was increased to 5.0%. The same result is shown with respect to the total cholesterol of plasma in Table IV of Jenkins. These results would cause a person skilled in the art to consider that the effect of lecithin on decreasing cholesterol concentration in serum and liver is not enhanced, even if the concentration of lecithin is increased.

Accordingly, it is respectfully submitted that Claims 18 and 35 - 36, 38 and 42 - 48 are not obvious over the Sugano references, Imaizumi, or Jenkins, alone or in combination.

Rejection of Claims 18 and 35 - 48 under 35 U.S.C. §103(a) over Sirtori in combination with Williams

Claims 18 and 35 - 48 were rejected under 35 U.S.C. §103(a) as obvious over Sirtori (Ann. Nutr. Metab. 1985) in combination with Williams. The Examiner alleges that

Sirtori teaches the effectiveness of lecithinated soy proteins in lowering cholesterol and that Williams teaches the effectiveness of phospholipids in cholesterol removal. The Examiner acknowledges that the amount of lecithin in the complex of Sitori is lower than the amount in the present invention. The Examiner alleges that it would have been obvious to vary the amounts of lecithin in the compositions of Sirtori because Williams teaches that phospholipids by themselves lower the cholesterol and Jenkins teaches that the level of dietary lecithin controls the effect of the source and type of protein on the lipid metabolism.

This rejection is respectfully traversed as it may be applied to Claims 18 and 35 - 36, 38 and 42 - 48 (Claims 37 and 39 - 41 having been canceled in the previous response). Although Sirtori teaches that a low-lipid diet with total replacement of animal proteins with textured soy proteins containing 6% of lecithin reduces serum total cholesterol, Sirtori is silent about the effect of a protein/phospholipid complex or protein hydrolyzate/phospholipid complex in which the content of bound phospholipid is from 20 to 50 wt%. Williams discloses that lecithin liposomes carry endogenous cholesterol to excrete endogenous cholesterol. However, Williams is silent as to whether the effect of lecithin liposomes would increase or not, when the amount of lecithin liposomes is increased.

Moreover, as discussed above, Jenkins teaches that the effect of lecithin is not enhanced, even if the concentration of lecithin is increased.

Therefore, Williams does not supply any motivation to vary the amounts of lecithin in the compositions of Sirtori.

Accordingly, it is respectfully submitted that Claims 18 and 35 - 36, 38 and 42 - 48 would not have been obvious over Sirtori and Williams, alone or in combination.

Rejection of Claims 18 and 35 - 48 under 35 U.S.C. §103(a) over Sirtori in combination with Williams and Jenkins

Claims 18 and 35 - 48 were rejected under 35 U.S.C. §103(a) as obvious over Sirtori in combination with Williams and Jenkins. The Examiner alleges that Sirtori teaches the effectiveness of lecithinated soy proteins in lowering cholesterol and that Williams teaches the effectiveness of phospholipids in cholesterol removal. The Examiner acknowledges that the amount of lecithin in the complex of Sitori is lower than the amount in the present invention. The Examiner alleges that it would have been obvious to vary the amounts of lecithin in the compositions of Sirtori because Williams teaches that phospholipids by themselves lower the cholesterol and Jenkins teaches that the level of dietary lecithin controls the effect of the source and type of protein on the lipid metabolism.

In response to the applicants' previous showing of nonobviousness and unexpected results in the declaration dated November 25, 2002, the Examiner alleges that the declaration is not persuasive because in Experiment I, only the amounts of lecithin in the complex are compared and not the amounts of phospholipid alone. The Examiner further alleges that the data in Table II appears to show an additive effect with regard to both serum cholesterol and liver cholesterol. The Examiner alleges that the prior art shows that soybean protein and lecithin each by itself has the ability to lower cholesterol and that an additive effect is expected and is not surprising. Secondly, the Examiner alleges that the studies described in the declaration were performed with only soybean protein and not with hydrolysates or wheat protein and are not commensurate in scope with "enzyme modified phospholipids or lecithin.

This rejection is respectfully traversed as it may be applied to Claims 18 and 35 - 36, 38 and 42 - 48 (Claims 37 and 39 - 41 having been canceled in the previous response). Although Sirtori teaches that a low-lipid diet with total replacement of animal proteins with textured soy proteins containing 6% of lecithin reduces serum total cholesterol, Sirtori is silent about the effect of a protein/phospholipid complex or protein hydrolyzate/phospholipid complex in which the content of bound phospholipid is from 20 to 50 wt%. Williams discloses that lecithin liposomes carry endogenous cholesterol to excrete endogenous cholesterol. However, Williams is silent as to whether the effect of lecithin liposomes would increase or not, when the amount of lecithin liposomes is increased.

Moreover, as discussed above, Jenkins teaches that the effect of lecithin is not enhanced, even if the concentration of lecithin is increased.

Therefore, Williams and Jenkins do not supply any motivation to vary the amounts of lecithin in the compositions of Sirtori.

Regarding the declaration submitted with the response of December 2, 2002, and the Examiner's comments thereof, the Examiner alleges that in experiment 1, there are no corresponding experiments with the same amounts of phospholipid alone to come to the conclusion that the results are synergistic. The Examiner also alleges that Table 2 does not show an effect of soybean protein and lecithin.

As an explanation of what is shown in the declaration, Figs. 1 and 2 show that when the content of bound phospholipid is 20 wt% or more, the effect of lowering cholesterol in serum and liver is critically improved. That is why data showing the effect of phospholipid alone was not given in Figs. 1 and 2. As mentioned below, the synergistic effect of the present invention is shown in Figs. 3 and 4 in the declaration.

As shown in Fig. 4 in the declaration, "Cholesterol in liver" is significantly decreased by feeding with the complex produced by binding protein to phospholipid, whereas "Cholesterol in liver" is slightly decreased by feeding protein, phospholipid and the mixture thereof. The effect of protein and phospholipid was enhanced by forming a complex thereof, whereas the effect was not enhanced by forming a mixture thereof. Thus, it was shown in this Figure that the effect obtained by a complex is synergistic.

Although one may be concerned that the result shown in Fig.3 does not show the effect of improving cholesterol metabolism, as explained below, in order to improve cholesterol metabolism, it is important to decrease the cholesterol concentration in liver and serum as a whole.

Cholesterol accumulated in liver is secreted to serum as lipoprotein. The secreted lipoprotein is a cause of increasing of cholesterol concentration in serum. If cholesterol is accumulated excessively in liver, cholesterol in serum is not longer taken into the liver to catabolize to bile acids. As the result, cholesterol that is not taken into the liver remains in the serum and disturbs the internal cholesterol metabolism. Thus, it is important to decrease the cholesterol level in the liver at a normal level in order to maintain the constancy of internal cholesterol metabolism. Enclosed is a reference showing transport of cholesterol (Harper's Biochemistry, twenty-fifth edition, page 291).

Therefore, the results shown by Figs.3 and 4 should be analyzed as a whole. When analyzing the results shown by Figs .3 and 4 as a whole, the results showed the synergistic effect of protein/phospholipid complex.

The Examiner also alleges that there are no data performed with hydrolyzate of soy protein, wheat protein or "enzyme modified phospholipids or lecithin". In response, Claims 18, 42 and 43 are amended so that the recited protein is limited to soybean protein.

As shown in the present specification and the declaration, Applicants have found that the complex of the present invention can improve cholesterol metabolism significantly. Since protein hydrolyzate is one of proteins, and enzyme-modified lecithin is one of phospholipids, protein/phospholipid complex, protein/enzyme—modified phospholipid complex, protein hydrolyzate/phospholipid complex and protein hydrolyzate/enzyme-modified phospholipid complex have the significant effect on improving cholesterol metabolism similarly. For example, as shown in Group 4 of Test Example 1, Group 6 of Test Example 2, and Group 9 of Test Example 3 of the present specification, the cholesterol metabolism-improving effects of protein/enzyme-modified phospholipid complex, protein hydrolyzate/phospholipid complex and protein hydrolyzate/enzyme-modified phospholipid complex containing 20 wt% of bound phospholipid or enzyme-modified phospholipid are the same or more than protein/phospholipid complex containing 20 wt% of bound phospholipid. Further, the significant effect of protein/phospholipid complex containing 50 wt% of bound phospholipid is shown in Figs. 1 and 2 of the declaration. Thus, the effect of improving cholesterol metabolism can be obtained even if the protein is hydrolyzed protein, or phospholipid is enzyme-modified phospholipid, so long as the complex contain 20-50 wt% bound phospholipid or enzyme-modified phospholipid.

Accordingly, it is respectfully submitted that Claims 18 and 35 - 36, 38 and 42 - 48 would not have been obvious over Sirtori, Williams, and Jenkins alone or in combination.

Conclusion

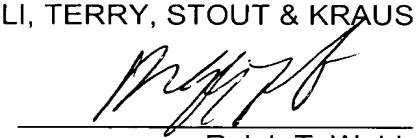
In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 18, 35, 36, 38, 42, 43, 44 and 48 are in condition for allowance. Favorable

reconsideration is respectfully requested.

Should the Examiner believe that anything further is necessary to place this application in condition for allowance, the Examiner is requested to contact applicants' undersigned attorney at the telephone number listed below.

Kindly charge any additional fees due, or credit overpayment of fees, to Deposit Account No. 01-2135 (506.35379CC2).

Respectfully submitted,
ANTONELLI, TERRY, STOUT & KRAUS



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Attachments:
Harper's Biochemistry, 25th edition,
page 291